Repeated Thrombus Formation Immediately Following Carotid Endarterectomy

—Case Report—

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Abstract

A 56-year-old male presented with thrombus formation manifesting as cerebral embolic infarction suspected to be caused by hemostasis at the carotid bifurcation, not by the intimal abnormalities or hematological disorders. Thrombus repeatedly and reproducibly appeared at the same area in spite of carotid endarterectomy (CEA). Ultrasonography demonstrated a stenotic lesion of the cervical carotid bifurcation. Medical treatment reduced the stenosis, but the thrombus was repeatedly formed at the same area of the cervical carotid bifurcation. CEA was performed. Histological examination of the specimen found only the underlying thin intima consisting of mild fibrous atheromatic change without ulceration or vascular dissection. Ultrasonography following CEA showed reduced blood flow, indicating hemostasis, and moyamoya appearance in that area. The thrombus had recurred in spite of the medical treatment with anti-platelet agent. This repeated thrombus was gradually dissolved and reduced with anticoagulant therapy. Thrombus causing cerebral embolic stroke and originating at the cervical carotid bifurcation is usually due to the intimal atherosclerotic change such as ulcer formation or vascular dissection. The thrombus in this case was probably formed by hemostasis at the cervical carotid bifurcation and CEA was not effective to prevent recurrence.

Key words: carotid endarterectomy, hemostasis, thrombus, moyamoya echo

Introduction

Carotid plaque appearing as hypoechoic on cervical ultrasonography is thought to be vulnerable and carry high risk, even if not severely stenotic, because the plaque contains lipid-rich content, thrombi, or necrotic tissue with high potential to cause cerebral embolic infarction.^{9,10)} Thrombus located at the cervical carotid bifurcation is usually caused by vascular intimal atheromatous change such as ulceration or dissection. Such thrombosis based on an abnormal vascular lesion may disappear after normalization of the intima by carotid endarterectomy (CEA). We treated a patient with cerebral embolic stroke who developed recurrent cervical thrombus without hypercoagulable or vascular atherosclerotic abnormalities.

Case Report

A 56-year-old male suffered abrupt onset of left hemiparesis and then lost consciousness while working. He was emergently transferred to our hospital by ambulance. Initial neurological examination showed moderate left hemiparesis, conjugated deviation to the right, and mild conscious disturbance. His blood pressure was 164/96 mmHg and heart rate was 54/min and regular. His past history included only hypertension.

Emergent magnetic resonance (MR) imaging showed relatively large cerebral infarction in the right temporal lobe and partially in the insula. MR angiography showed a saddle disappearance of the inferior division (M₂) of the right middle cerebral artery. Single photon emission computed tomography also detected severe low perfusion in the same region. Cerebral embolism was suspected based on the clinical presentation. Electrocardiography and echocardiography found no abnormalities. Laboratory data were also within the normal range includ-

Fig. 1 A: Ultrasonogram performed before operation showing a hypoechoic mass at the cervical carotid artery. B, C: Ultrasonogram (B) and right carotid angiogram (C) one week later showing reduction of the mass. D: Ultrasonogram performed out of warfarin control showing re-increase of the hypoechoic mass up to approximately 60% stenosis in the same area.

ing platelet count and coagulative functions such as protein C, protein S, and lupus anticoagulant. There were no signs of hypercoagulation state.

He was medically treated with sodium ozagrel, an inhibitor against thromboxane A_2 . His neurological findings gradually improved, besides disorientation, discalculation, and short memory disturbance. On the 3rd day of admission, ultrasonography (Aloka SSD 2200; Aloka Co., Ltd., Tokyo; with 7.5 MHz probe) detected a hypoechoic mass located at the right cervical carotid bifurcation, estimated as approximately 50% stenosis (Fig. 1A). However, on the next day carotid angiography unexpectedly showed disappearance of this moderate cervical carotid stenosis and only a slight prominence with a shallow dent (Fig. 1C). Repeat ultrasonography also did not detect any stenotic lesion, ulceration, or dissecting lesion at the same area (Fig. 1B). These results indicated that the lesion of the cervical carotid artery may have induced cerebral embolic infarction. Anticoagulant therapy using warfarin was performed to prevent recurrence of thrombus.

Medication with warfarin was controlled by referring to the values of the thrombo test (TT) and international normalized ratio (INR) of activated partial

thromboplastin time. When the medication was stopped for only a few days, because the values exceeded the appropriate range, the lower value of TT and the raised value of INR instantaneously returned to normal. Cervical ultrasonography, performed when TT was still high and INR was low, showed a reproducible re-increase in the hypoechoic mass up to approximately 60% stenosis in the same area as previously (Fig. 1D). However, a more effective dose of warfarin gradually decreased the stenotic hypoechoic prominence to 30% stenosis. The increase in the thrombus was believed to be induced by an atherosclerotic intimal abnormality, such as mild ulceration of the carotid artery, which cervical carotid angiography identified as a mild dent.

CEA was planned for the right carotid artery to prevent recurrence and re-increase of thrombus. Intraoperative observation revealed only a tiny atherosclerotic plaque on the carotid lumen at the lateral wall of the carotid bifurcation and a thin clot just attached to the intima with normal appearance. The intima was too thin and firm to be peeled out easily (Fig. 2A, B). The underlying layer did not show ulceration or dissection. Histological examination showed organized thrombus on the slightly fibrous atherosclerotic intima and no ulcerative change of the intima (Fig. 2C).

After surgery, ticlopidine, an anti-platelet agent, was given to prevent the formation of thrombus. His postoperative course was excellent and cervical ultrasonography detected no recurrence of thrombus. However, drifting moyamoya (smoke-like) appearance (called moyamoya echo) was observed just around the area where the thrombus had formed (Fig. 3A), and power Doppler and color Doppler ultrasonography revealed reduced blood flow shaped like a wedge at the same area, despite detecting no obstructions in the lumen since the 15th postoperative day (Fig. 3B, C). These observations suggested hemostasis. Ultrasonography detected no new thrombus formation at the cervical bifurcation. He was discharged from the hospital on the 29th postoperative day, under ticlopidine medication.

Unexpectedly cervical ultrasonography (Philips Sonos 5500; Philips Medical Systems, Best, The Netherlands; with 3–11 MHz probe) undertaken 2 weeks after discharge showed re-growth of the hypoechoic mass at the same wedge-shaped area suggested to be hemostasis, but without neurological symptoms (Fig. 3D). The mass was estimated as up to 50% stenosis. Immediately, he was re-admitted and treated with heparin 15,000 U/day, followed by warfarin to prevent embolic infarction instead of ticlopidine administration. During the anticoagulant

Fig. 2 A: Intraoperative photograph showing thin thrombus attached to the intima, with just partial mild atherosclerotic change. B: Photograph of the divided face of the specimen showing the underlying layer of a thin thrombus over thin normal intima. C: Photomicrograph showing an organized thrombus on the mild atherosclerotic intima, not associated with ulcerative change. HE stain, $\times 20$.

Fig. 3 A: Postoperative ultrasonogram showing no stenotic lesion, but moyamoya appearance (arrowheads). B, C: Power Doppler (B) and color Doppler ultrasonograms (C) showing reduction of the blood flow, indicating hemostasis. D: Ultrasonogram 2 weeks after discharge showing recurrence of the hypoechoic mass. E: Ultrasonogram demonstrating gradual reduction of thrombus under warfarin control.

therapy, ultrasonography showed the thrombus was gradually reduced below approximately 30% stenosis (Fig. 3E). He has not experienced new neurological symptoms or new ischemic lesion by neuroradiological examinations. He was discharged from our hospital, under warfarin medication and stabiliza-

tion of the cervical region.

Discussion

Stenotic prominences of the cervical carotid artery, usually caused by fibrous atheromatous plaque and calcification, induce several types of pathogenesis resulting in cerebral ischemia. Atheromatic plaque consists of connective tissue extracellular matrix, lipid content-like cholesteryl ester, inflammatory cells, and necrosis. Individual differences in the component proportions lead to various pathogeneses, which include formation of thrombus or embolus, or disturbance of the established collateral flow as well as critical reduction of the cerebral blood flow. Treatment planning must discriminate the pathogenic mechanism as well as the components of the prominence causing cerebral infarction.

The pathogenesis in our patient was suspected to be embolic, but several investigations of the source of embolism failed to discover any mural thrombus, cardiac diseases, or blood cell disorders with hypercoagulability, excluding the cervical carotid lesion. Paradoxical embolism is a rare cause of stroke,⁸⁾ but patients with stroke may have a patent foramen ovale, suggesting investigation of intracardiac disorders.⁷⁾ Our patient did not have any cardiac disorders, but thrombus was repeatedly found at the cervical bifurcation by ultrasonography following CEA and before the anticoagulant therapy had become effective. Clot formation usually originates at an intimal abnormality such as ulceration and vascular dissection caused by atheromatous plaque, or as a kind of hematoma in the arterial wall exposed by progression of the ulceration or decaptinizing of the atheromatous cap. Both mechanisms are caused by the underlying atheromatous change. Thrombus unrelated to the atheromatous plaque in the cervical carotid artery has been reported in only five cases, possibly originating in valvular strands on the aortic valve, thrombocytopenia, and anemia.^{1,4)} All cases including our case could exclude the underlying vascular atheromatous lesion of the cervical carotid artery. Our case did not have known causes such as cardiac and hematological disorders, and furthermore recurred, so this type of thrombus is extremely rare.

CEA is effective for treating problems of the cervical carotid artery compared with the medical treatment.^{2,5)} The North American Symptomatic Carotid Endarterectomy Trial study recognized that thrombus formation in the carotid artery was one of the factors that raise the risk of perioperative stroke and death. We selected this surgical procedure to imme-

diately avoid embolic risk as well as to remove the underlying atherosclerotic plaque.²⁾ In our case, the cause of thrombus formation was initially considered to be mild change in the atherosclerosis, as indicated by carotid angiography. However, the operative findings revealed the atheromatous plaque was tiny and located at the side of the thrombus. The thin thrombus also only just touched the vascular intima which looked almost normal. The histological findings also showed only tiny atheromatous plaque and thrombus, not associated with ulceration or dissection. Moreover, the thrombus reappeared at the same area following CEA, despite antiplatelet treatment. These findings suggested that only the abnormality of the intima was not sufficient to induce formation of the thrombus at the cervical carotid bifurcation. Therefore, the cause of the thrombus remained unclear.

Cervical ultrasonography can detect any abnormality of the cervical carotid artery. This method is convenient, reproducible, and accurate, as well as less invasive.⁶⁾ In particular, the information on the content of the cervical carotid stenotic lesion is better than that given by angiography, MR imaging, or three-dimensional computed tomography. Ultrasonography is now essential in considering treatment for these lesions at the carotid bifurcation. Generally, a hypoechogenic appearance indicates lipid accumulation, necrosis, and thrombi.^{9,10)} In our case, the hypoechoic prominence without other echoic areas suggested the presence of only thrombus. Following CEA, power Doppler and color Doppler ultrasonography showed reduced blood flow in the same area, suggesting hemostasis of blood flow. Furthermore, moyamoya (smoke-like) appearance often associated with thrombus formation in the heart³⁾ was detected at the same area. The faint drifting or flowing echo is highly indicative of thrombus, but the basic cause of the moyamoya appearance still remains unclear. In these situations, one cause of thrombus formation may be hemostasis of blood flow at the cervical bifurcation. The mechanism of hemostasis is unclear, but may be caused by the complicated tangle of the anatomical structure, e.g. the angle, the diameter, and the velocity and viscosity of blood flow, as well as the state of the intima at the carotid bifurcation. Hypercoagulable syndrome and hematological diseases, although excluded in this patient, might also be related to this situation because anticoagulant therapy with warfarin was finally effective to reduce the thrombus in this patient.

Ultrasonography and MR imaging should be performed to assess stenosis of the cervical bifurcation. Evidence of thrombus indicates that medical

treatment as well as surgical therapy such as CEA should be considered.

Acknowledgment

We greatly appreciate Miss Mutsuko Muraki's technical contribution in echo examination and the analysis.

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